UNDERSTANDING A PEDIATRIC GOOD DEATH IN THE AGE OF MEDICAL INNOVATION

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Abstract

In the last two decades, significant progress has been made to increase the number of life-saving therapies for pediatric populations. This medical innovation provides tremendous benefit and hope to children with life-limiting and life-threatening diseases and their families, as well as to physicians, researchers, industry, and society more broadly. While the potential benefits derived from experimental treatments provide motivations for parents to seek these treatments for their child, it is important to recognize that the uncertainty associated with early stage experimental therapies brings with it potential for harm. One such harm is depriving the child of a good death.

In this paper, I will explore the concept of a good death and how it applies in the pediatric context. I will consider if current frameworks of a pediatric good death sufficiently account for the added uncertainty, benefits and harms associated with early stage medical innovation and how these benefits and harms may impact parents' decision making. Despite the potential for harm, it is impossible to ignore the significant personal and societal benefits of experimental medicine. While every pediatric end-of-life experience must be evaluated individually, it is essential that all parents and physicians considering experimental medicine adequately account for the potential harms, particularly the potential of preventing a good death.

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Introduction

Although death is most commonly recognized as a harm, it is essential to understand what makes a good death, especially in the age of medical innovation. This question is particularly fraught in the pediatric context. Many conceptions of a pediatric good death inadequately prioritize the interests of the child, particularly as patients must consider pursuing experimental treatments or medical innovation. The balance of the ethical principles of beneficence, non-maleficence, and autonomy is complicated by the uncertainty that can exist in these situations. Additionally, infants and toddlers lack autonomy, and their medical decision-making is shaped by the interests of their parents, community, and care team. These patients cannot themselves consent to the risks associated with experimental treatments, and parents may be swayed by the hope for significant therapeutic benefit in addition to the contribution to scientific knowledge. It is necessary to consider how to protect the good death for a child, while at the same time recognizing the interwoven nature of the parents' interests, as well as the need to continue to drive science forward.

The Age of Medical Innovation

The passage of the Pediatric Research Equity Act (2003) and The Best Pharmaceuticals for Children Act (2002), created incentives for the development of pediatric therapies as well as the exploration of repurposing already approved adult treatments for children.[1] Currently 2,100 clinical trials are testing almost 600 drugs for use in pediatric populations.[2] In addition to the development of drugs and biologic therapies through clinical trials, there continues to be variation from standard protocol in fields like surgery to advance the field and develop new

[1] PhRMA, "Medicines in Development for Children 2020 Report," 2020.
[2] PhRMA.

effective treatments.[3] As a result, more patients with conditions that lack approved treatments, or have been unresponsive to the standard of care, are presented with experimental options for their treatment.[4] The term *experimental treatments* can mean many things, from early stage clinical trials with drugs never before tested in humans, to innovation at the bedside that is outside standard clinical protocol, but does not require regulatory oversight.[5] Without this innovation, children with life limiting conditions would likely continue to suffer and die prematurely from causes that show potential for treatment as science and technology progress.

All medical treatments and procedures maintain some level of risk. While patients must always consider a risk-benefit analysis, this is particularly difficult when both the potential risks and benefits are to some extent unknown. While pre-clinical studies and animal models establish the scientific basis for pursuing a particular treatment in humans, phase I trials entail unforeseen risk and unknown benefit.[6] Phase I trials are the first time a specific drug is tested in humans. The purpose of these trials is to determine the maximum tolerated dose, or the dose before toxicity appears in trial participants. It is important to note that the intended goal of a phase I study is not therapeutic. This creates "a risk that subjects who volunteer (or the actual physicians who enroll patients) for phase I studies will misinterpret its objective as therapeutic" and enroll for the wrong reasons.[7] Phase II trials "are designed to test safety, pharmacokinetics, and pharmacodynamics but may also be designed to answer questions essential to the planning of

[3] Jennifer A.T. Schwartz, "Innovation in Pediatric Surgery: The Surgical Innovation Continuum and the ETHICAL Model," *Journal of Pediatric Surgery* 49, no. 4 (April 2014): 639–45, https://doi.org/10.1016/j.jpedsurg.2013.12.016.
[4] Alan R. Fleischman and Lauren K. Collogan, "Research with Children," in *The Oxford Textbook of Clinical Research Ethics*, 1. iss. as an OUP pbk (Oxford: Oxford Univ. Press, 2011).
[5] Ran Svenning Berg, "Patient Access to Experimental Treatments" (Nuffield Council on Bioethics, November 20, 2018), https://www.nuffieldbioethics.org/publications/experimental-treatments.
[6] Craig A. Umscheid, David J. Margolis, and Craig E. Grossman, "Key Concepts of Clinical Trials: A Narrative Review," *Postgraduate Medicine* 123, no. 5 (September 2011): 194–204, https://doi.org/10.3810/pgm.2011.09.2475.
[7] Umscheid, Margolis, and Grossman.

phase III trials, including determinations of optimal doses, dose frequencies, administration routes, and endpoints."[8] During phase II trials, researchers are only beginning to test for therapeutic effectiveness. If the drug demonstrates potential efficacy, a phase III trial is pursued to "demonstrate and/or confirm efficacy and to identify and estimate the incidence of common adverse reactions."[9] In each stage of the drug development process, there is some level of risk to research participants. It is also worthwhile to note that only 13.8% of drugs and vaccines that begin clinical trials complete the process and receive U.S. Food and Drug Administration approval.[10] For oncology, this rate is even lower at 3.4%.[11]

For the context of this paper, *experimental treatments* refers to new treatments and protocols with greater than minimal risk both with and without prospect of direct benefit to the subject as designated by the Code of Federal Regulations. While these initial stages are necessary to progress toward safe and effective treatments, they come with uncertainties that must be taken into account. Innovation brings tremendous hope and possibility to children with life-limiting diseases and to their families, and more broadly to physicians, investigators, industry and society. The protectionist nature of experimental treatments notwithstanding, some level of uncertainty persists. Dr. Florian Eichler, a pediatric neurologist at Massachusetts General Hospital articulates this well saying, "That is the nature of progress. If we knew what works, we wouldn't need to conduct trials."[12]

In addition to the unknown outcomes and potential physical risks related to the

[8] Umscheid, Margolis, and Grossman.
[9] Umscheid, Margolis, and Grossman.
[10] Chi Heem Wong, Kien Wei Siah, and Andrew W Lo, "Estimation of Clinical Trial Success Rates and Related Parameters," *Biostatistics* 20, no. 2 (April 1, 2019): 273–86, https://doi.org/10.1093/biostatistics/kxx069.
[11] Wong, Siah, and Lo.
[12] Karen Weintraub, "An Experimental Gene Therapy Was Little Alissa's Only Hope. Now, Instead of Certain Death, She Faces an Uncertain Future.," *USA TODAY*, April 25, 2021, https://www.usatoday.com/in-depth/news/health/2021/04/25/gene-therapy-offers-hope-danish-girl-but-uncertainty-lies-ahead/4850987001/.

experimental treatment itself, there are other potential costs associated with pursuing them. These can include, but are not limited to, time lost at hospitals and appointments, diminished quality of life, and decreased ability to create a positive end-of-life experience. I must note that these costs are not definite and each family experiences end-of-life treatment differently. However, it is worth considering that experimental treatments may increase the likelihood of these negative costs for some families. Furthermore, access to experimental treatments is limited and only available in specific treatment centers, trial locations, or by specific providers. This leads many families to relocate at additional costs to both their financial and social wellbeing.[13] One potential cost of experimental treatments is depriving the child of a good death.

Is Death Inherently Bad?

To fully understand the tension between experimental treatments and a good death, we must first come to the conclusion that death is inherently bad and something to avoid. This conclusion informs to what extent we should work to delay death with experimental treatments. Death and dying is widely discussed in philosophical literature, and many commentators conclude that death can only be bad if life is accepted as a good or positive experience. This is not to say that there are not negative aspects to life. It is clear that there are diverse life experiences in all dimensions of life, some of which are negative. To truly understand if death is bad for someone, "we must compare her actual welfare level to the welfare level she would have had if she had not died."[14] As life progresses, this calculation can become much more difficult. However, when considering this calculation for a child, one can assume there is a great possibility for increasing welfare over the course of their life. This would suggest that the death

[13] Karen Weintraub.
[14] Steven Luper, "Death," in *The Stanford Encyclopedia of Philosophy*, ed. Edward N. Zalta, n.d., https://plato.stanford.edu/archives/win2019/entries/death/.

of a child would diminish welfare and be bad for that child. However, it is truly impossible to know what the outcome would be because we can never know how a person's life were to progress should they not have died.

Furthermore, this calculation is not straightforward and differs for each child and condition. For example, the parents of a typically developing 3-year-old may be more inclined to pursue experimental treatments in a hope to prevent death because they have a better understanding of what their child's life could look like should the treatment prove curative. On the other hand, we can see how this decision can be much more complicated in the case of a progressive and fatal neurodegenerative disorder, as in the case with Thomas Feldborg, Daria Rokina, and their daughter Alissa. While an experimental gene therapy exists for Alissa's condition, it remains unclear to what extent it will halt progression or restore function. It is similarly uncertain what physical and intellectual capabilities Alissa will have following treatment or if the treatment will prevent the painful symptoms of her condition. Moreover, there are potential risks associated with the treatment itself. Feldborg worries that "Instead of having this cruel, short life of two, three, maybe four years, maybe she will just have a cruel, long life."[15] A situation like Thomas, Daria, and Alissa's conveys the complexity around death and raises questions as to whether premature death reduces welfare for a child with severe illness that causes significant pain, suffering, and disability. While there are many complexities that cause some to question if death is always bad, it is difficult to ignore the significant potential that

[15] Karen Weintraub, "An Experimental Gene Therapy Was Little Alissa's Only Hope. Now, Instead of Certain Death, She Faces an Uncertain Future."

exists in a child. This premature death, of whatever cause, prevents the child from "the only life the particular child will ever experience."[16]

Though death is an inevitable part of the human experience, it is clear that a child's death goes against the natural order of life and most parents do not anticipate watching their child die,[17] in part due to the potential and future that is lost. Accordingly, I will move forward in this paper with the understanding that life should be valued and the death of a child is a particularly tragic outcome that should be prevented, unless the costs of doing so cause more harm to the child.

The Good Death

Although death is a harm that cannot be avoided, it is helpful to understand what makes a good death to ensure that the dying process does not create additional harms. While most people would agree that assisting someone to have a good death ought to be the goal, we must acknowledge that "good" is a value judgement that cannot be easily made. There exist different conceptions of what is good and what is not, and these beliefs are shaped by cultural and social factors. Recognizing that many individuals have different understandings of what a good death looks like, significant work has been done to understand what a good death, or successful dying, means for adult patients.

The Institute of Medicine, now the National Academy of Medicine, described a good death as "free from avoidable distress and suffering for a patient, family, and caregivers, in general accord with the patient's and family's wishes, and reasonably consistent with clinical,

[16] David N Cornfield and Jeffrey P Kahn, "Decisions about Life-Sustaining Measures in Children: In Whose Best Interests?: End of Life, Paediatrics," *Acta Paediatrica* 101, no. 4 (April 2012): 333–36, https://doi.org/10.1111/j.1651-2227.2011.02531.x.
[17] Silvana Barone and Yoram Unguru, "Ethical Issues Around Pediatric Death," *Child and Adolescent Psychiatric Clinics of North America* 27, no. 4 (October 2018): 539–50, https://doi.org/10.1016/j.chc.2018.05.009.

cultural, and ethical standards."[18] In an attempt to bring clarity and a useful structure to definitions like these, Ezekiel Emanuel and Linda Emanuel developed a framework for assessing the quality of a death. The framework views death as a multidimensional experience and includes four central components: "1) the fixed characteristics of the patient; 2) the modifiable dimensions of the patient's experience, or elements that may respond to events or interventions; 3) the potential interventions available to family friends, health-care providers and others; and 4) the overall outcome."[19] The framework exists with the understanding that there is more to a good death than the physical symptoms. There are significant social and emotional components to death as well. The framework focuses on the preferences of the patient and identifies where various interventions can be implemented to improve the quality of the dying process.[20] While Emmanuel and Emmanuel have a strong focus on alleviating suffering, they acknowledge that there are many aspects of dying beyond pain that must be considered. They also stress that the patient's support network should strive to meet the patient's preferences for the dying process.

Recognizing the general preferences of what matters to dying patients is an extensive undertaking requiring significant qualitative study. Emily Meier et al. conducted a literature review to develop a comprehensive understanding of what a good death meant to adult patients and evaluated patients' preferences. The review includes 36 articles "published in English in peer-reviewed journals and provided quantitative or qualitative data that specifically defined or used a measure of good death as the main aim or outcome of the study."[21] The studies included

[18] *Approaching Death: Improving Care at the End of Life* (Washington, D.C.: National Academies Press, 1997), https://doi.org/10.17226/5801.
[19] Ezekiel J Emanuel and Linda L Emanuel, "The Promise of a Good Death," *The Lancet* 351 (May 1998): SII21–29, https://doi.org/10.1016/S0140-6736(98)90329-4.
[20] Emanuel and Emanuel.
[21] Emily A. Meier et al., "Defining a Good Death (Successful Dying): Literature Review and a Call for Research and Public Dialogue," *The American Journal of Geriatric Psychiatry* 24, no. 4 (April 2016): 261–71, https://doi.org/10.1016/j.jagp.2016.01.135.

in the review were primarily conducted in the United States and United Kingdom, but also included studies conducted in the following countries: Japan, Netherlands, Thailand, Iran, Israel, Canada, Nova Scotia, Saudi Arabia, South Korea, Sweden, and Turkey. Meier et al. identified 11 core themes of a good death, including preferences for a specific dying process, pain-free status, religiosity/spirituality, emotional well-being, life completion, treatment preferences, dignity, family, quality of life, relationship with [healthcare providers], and other. The top three themes across all stakeholder groups were preferences for dying process (94% of reports), pain-free status (81%), and emotional well-being (64%).[22]

Despite death being viewed as a harm, this review is helpful to understand what makes a good death in aging populations. However, at least four of these eleven themes (preferences for a specific dying process, life completion, treatment preferences and religiosity/spirituality) are not possible to meet for very young pediatric patients, leaving gaps for understanding a good death in the pediatric context. While the adult literature can be useful even though core criteria in the adult context are not achievable in all pediatric cases, it remains important to determine whether a pediatric good death is possible. Should a pediatric good death be possible, we must characterize what it looks like so we can act in alignment and reduce potential harms.

A Pediatric Good Death

It is important to note that the phrase *pediatric patients* can refer to a large span of developmental ages from neonates to minors on the cusp of adulthood. This paper focuses on infants and toddlers who do not yet have an understanding of life and death and the possibility for shared decision-making is limited. In much of the literature surrounding a good death for

[22] Meier et al.

adult patients, a great deal of what makes a death good is how well it aligns with the patient's preferences for the dying process. This fundamental criterion is not always applicable to infants and toddlers since they have yet to truly live and do not have their own preferences for how they would like to die. However, it is important to acknowledge that young children, particularly those enduring serious illness, often have more capabilities to understand their medical situations than many people appreciate.[23] Though they may require specialized, developmentally appropriate communication methods, children around age four years can actively partake in their healthcare.[24] Without diminishing the experience and abilities of children, we must still acknowledge that many pediatric patients are not able to fully comprehend what is happening to them. It is particularly important to explore what a good death means for these children because "by definition, children cannot advocate for themselves" and their parents or other caregivers are not always in a position to see the situation clearly due to grief, pain, fear, or anger.[25]

As children mature and can begin to express their opinions and desires, but are not yet fully autonomous, the situation changes again to a different, but still uniquely complex one. In the case of older children who can begin to express their desires and understand the situation, many would advocate for a shared decision-making model.[26] Shared decision-making involves including the child in a developmentally appropriate way rather than allowing their interests to be a secondary concern. However, most pediatric deaths occur in the first year of life, making

[23] Lynn Hagger and Simon Woods, eds., *A Good Death? Law and Ethics in Practice* (Farnham, Surrey, England ; Burlington, VT: Ashgate, 2013).
[24] Hagger and Woods.
[25] Marilyn J. Field, Richard E. Behrman, and Institute of Medicine (U.S.), eds., *When Children Die: Improving Palliative and End-of-Life Care for Children and Their Families* (Washington, D.C: National Academy Press, 2003).
[26] Jonathan Santoro and Mariko Bennett, "Ethics of End of Life Decisions in Pediatrics: A Narrative Review of the Roles of Caregivers, Shared Decision-Making, and Patient Centered Values," *Behavioral Sciences* 8, no. 5 (April 26, 2018): 42, https://doi.org/10.3390/bs8050042.

shared decision making impossible.[27] In addition to very young pediatric patients being unable to participate in shared decision-making, "pediatric patients with diminished cognitive, motor, or language capacities similarly lack the ability to participate" in this type of collaborative care.[28] Because shared decision-making is not an option and there are not many studies exploring end-of-life decision-making in these instances, some turn to the experience of adults with diminished capacity through dementia or cognitive decline as an example.[29] However, proxy decision makers in these cases strive to make decisions as though they were the patient, using knowledge about the patient's former preferences, goals, and desires.[30] Children who have yet to truly live do not have preferences for how they would like to die, especially if they never had the cognitive abilities to truly develop or express these preferences to begin with.[31] Consequently, a framework for a pediatric good death that prioritizes the interests of the patient must be identified.

Many have tried to bridge the gap between the idea of an adult good death and a pediatric good death. There are several studies, frameworks, and perspectives that provide some context for the current views of a pediatric good death. Christine Fortney and Deborah Steward published *A New Framework to Evaluate the Quality of a Neonatal Death* in 2014. This framework identifies the gaps in the literature between adult and pediatric end-of-life care and recognizes that existing studies on end-of-life care in the neonatal intensive care unit (NICU) focused primarily on the interests of the child's caregivers and loved ones.[32] This framework

[27] *Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life* (Washington, D.C.: National Academies Press, 2015), https://doi.org/10.17226/18748.
[28] Santoro and Bennett, "Ethics of End of Life Decisions in Pediatrics."
[29] Santoro and Bennett.
[30] Santoro and Bennett.
[31] Santoro and Bennett.
[32] Christine A. Fortney and Deborah K. Steward, "A New Framework to Evaluate the Quality of a Neonatal Death," *Death Studies* 38, no. 5 (May 28, 2014): 294–301, https://doi.org/10.1080/07481187.2012.742475.

identifies three domains: infant, parent, and nurse, which all interact and affect the dying process and the quality of death. Both fixed and modifiable characteristics exist within the infant domain and influence the dying process. The framework acknowledges that the modifiable dimensions from Emanuel and Emanuel (1998)'s framework do not adequately encompass all the modifiable characteristics of a neonatal patient. Unlike adult patients, "infants communicate symptoms through changes in physiologic indicators and behavioral cues, relying on others to accurately interpret their symptoms and advocate for relief" so it is imperative that providers in the NICU observe the infant's physical appearance which is "driven by behavioral and physiologic cues."[33] Because young children cannot directly communicate their symptoms, physical appearance is one element that plays an essential role in the pediatric context.

Under the Fortney and Steward framework, the parent domain represents one third of the equation. There are many situations when additional care is considered medically ineffective and "parents must refocus their role from assisting their infant survive to assisting their infant die."[34] It is often the parents who experience the child's death as either positive or negative, so it is critical that they are supported in the process as well.[35] The final domain is the nurse domain. While physicians oversee the care occurring in the NICU, nurses often have the most direct interaction with the infant and are particularly suited to understand various cues and symptoms. In addition to the parent's perception, the nurses' perceptions of these symptoms are factored in identifying the quality of the patient's death. Overall, this framework balances the infant, the parents, and the nurse's experience to evaluate the quality of the infant's death.

Another framework proposed by Elizabeth Broden et al. focuses on defining a good death

[33] Fortney and Steward.
[34] Fortney and Steward.
[35] Fortney and Steward.

in the pediatric intensive care unit (PICU). Broden and colleagues acknowledge that due to "the profound and enduring nature of parents' grief, integrating their perspectives into the definition of a good death in the PICU is imperative."[36] This framework evaluates the quality of a child's death by assessing the antecedents, the attributes, and the consequences of a good death.[37] The antecedents of a good death include "communication, preparation, mutuality, and resource mobilization." The consequences of a good death include the "bereavement experience, adaptation, and continued bonds and memories."[38] According to Broden et al, "a good death in the PICU is therefore defined as one in which the dying child receives optimal clinical care from a compassionate, respectful, and communicative multidisciplinary staff, and patient and family situational and psychosocial-spiritual needs are identified and met."[39] While this framework ensures the patient receives optimal care and the family's needs are met, it does not do enough to address the potential for suffering resulting from some attempts at providing so-called "optimal" care. Optimal may be viewed differently by different parents. Some parents view optimal care as doing anything possible to extend life whereas others understand optimal care as following standard of care or reducing suffering.

Taylor et al. explored what healthcare providers (HCPs) working in pediatric oncology at Seattle's Children's Hospital defined as a good death for their patients. This study attempted to find an empirical description of a good death for pediatric patients to help improve the quality of end-of-life and palliative care.[40] This mixed methods study identified open communication and

[36] Elizabeth G. Broden et al., "Defining a 'Good Death' in the Pediatric Intensive Care Unit," *American Journal of Critical Care* 29, no. 2 (March 1, 2020): 111–21, https://doi.org/10.4037/ajcc2020466.
[37] Broden et al.
[38] Broden et al.
[39] Broden et al.
[40] Mallory R. Taylor et al., "Defining a 'Good Death' in Pediatric Oncology: A Mixed Methods Study of Healthcare Providers," *Children* 7, no. 8 (July 31, 2020): 86, https://doi.org/10.3390/children7080086.

expert pain and symptom management as themes consistent with good end-of-life care.[41] Aside from "a small number of explicit examples of HCPs contrasting that what was 'good' for the family was not necessarily 'good' for the provider team," generally providers viewed a death as good if it aligned with the family wishes.[42]

Chong and colleagues conducted a review to evaluate the perceptions of a good death for children with life-shortening conditions from various viewpoints. The three major themes identified were "level of needs," "the composite experience," and "control."[43] A tentative model was developed to understand end-of-life care for pediatric patients. In this model, the sphere of influence, "refers to the entire healthcare context…within which stakeholders interact."[44] Within this sphere, all of the stakeholders may have different needs, experiences, and control. How all of these stakeholders interact contributes to the death of the child by "determining the extent of suffering at any point in time."[45] Chong and colleagues "[postulate] here that the measure of a good death is inversely related to the perception of suffering."[46] With this understanding of a good death, the child's well-being and experience can be prioritized to reduce suffering as much as possible. This is particularly important when parents felt a need to maintain hope, even with a poor prognosis. Maintaining hope for a cure was a prominent theme across all focus groups, even at the end stages of life. Families described the ability to hold on to two dichotomous beliefs: the realism that their child's prognosis was poor and the search for a miracle.[47] This finding supports

[41] Taylor et al.
[42] Taylor et al.
[43] Poh Heng Chong, Catherine Walshe, and Sean Hughes, "Perceptions of a Good Death in Children with Life-Shortening Conditions: An Integrative Review," *Journal of Palliative Medicine* 22, no. 6 (June 2019): 714–23, https://doi.org/10.1089/jpm.2018.0335.
[44] Chong, Walshe, and Hughes.
[45] Chong, Walshe, and Hughes.
[46] Chong, Walshe, and Hughes.
[47] Chong, Walshe, and Hughes.

work by Bryan Sisk and colleagues on characterizing the experience of parental hope in pediatric oncology. Both suggest that hope is a multidimensional concept and hope for a cure is only one element of parental hope.[48]

Chong et al. consider the tension that exists between reducing suffering and providing extreme measures to extend life at all costs.[49] This point should remain at the forefront of the medical decision-making process as we enter an age of scientific advancement, increased experimental options, and technology that can extend life in potentially harmful ways. With this in mind it is necessary to understand "that intensive care treatment is not a goal in itself. Its aim is not only survival of the [patient], but also an acceptable quality of life."[50]

As intensive care becomes more advanced and parents are faced with increasing numbers of experimental therapies, the question of a pediatric good death becomes increasingly more urgent. All the frameworks mentioned provide important insight to what makes a pediatric good death and they highlight how integral the experience of the parent is to the dying process. However, they also suggest that it is quite easy for the interests of the child to be superseded by the interest of others. This is particularly pertinent in the context of experimental therapies because they add additional interests to the decision-making process: increased hope and broad scale scientific advancement. Those making treatment decisions must recognize how these added benefits impact the cost-benefit analysis and the role these benefits play in the decision-making process. As more options become available to try to save a child, it is crucial that we begin exploring how to best balance the tensions between doing everything while at the same time

[48] Bryan A. Sisk, Tammy I. Kang, and Jennifer W. Mack, "Sources of Parental Hope in Pediatric Oncology," *Pediatric Blood & Cancer* 65, no. 6 (June 2018): e26981, https://doi.org/10.1002/pbc.26981.
[49] Chong, Walshe, and Hughes, "Perceptions of a Good Death in Children with Life-Shortening Conditions."
[50] Eduard Verhagen and Pieter J.J. Sauer, "The Groningen Protocol — Euthanasia in Severely Ill Newborns," *New England Journal of Medicine* 352, no. 10 (March 10, 2005): 959–62, https://doi.org/10.1056/NEJMp058026.

causing the least suffering possible.

Balancing the Interests of the Patient and the Parent

Even with the significant scholarship to understand a good death in the pediatric context, we still must consider if and how medical innovation plays a role. Because young children cannot consent to medical treatment or participate in shared decision-making, parents are tasked with making decisions that are in the best interest of the child. The best interest standard (BIS) is understood as "acting so as to promote maximally the good (i.e., well-being) of the incompetent individual."[51] In *Deciding for Others: The Ethics of Surrogate Decision Making,* Allen Buchanan and Dan W. Brock explore the concept of using the best interest standard as a guidance principle in pediatric decision-making. When adult patients are incapacitated or incompetent, a proxy decision maker steps in. In these situations, the proxy is expected to act on the interests and values expressed by the patient at a time when they were competent. The patient's existing values guide the proxy's decision-making. However, young children and children with significant developmental disabilities do not have their own values or understanding of the world. It is for this reason that pediatric decision-making is unique and Buchanan and Broch argue that the best interest standard is the appropriate guidance principle.

For young pediatric patients, the best interest standard is employed in medical decision-making, including end-of-life decisions. However, there are two aspects that make applying BIS less straightforward in end-of-life situations. First, there is not always consensus about what is in the best interest of the child. While conflict over what is in a child's best interest exists in other circumstances, stakes are much higher in end-of-life situations. As discussed above, this

[51] Allen E. Buchanan and Dan W. Brock, *Deciding for Others: The Ethics of Surrogate Decision Making* (Cambridge [England] ; New York: Cambridge University Press, 1989).

conversation occurs with the understanding that death is a bad thing and is particularly bad for children. With this in mind and despite potential consequences, some parents desire to extend life as long as possible. Some commentators would argue that the consequences and potential outcome should not be the predominant element in the decision-making process because, as articulated by David Cornfield and Jeffery Kahn, "a critically ill child cannot trade its current life for a different healthier life…. Whatever limitations and disabilities may result, the life in question is the only life the particular child will ever experience."[52] This could lead some parents to make decisions to choose unapproved treatments without fear of the outcomes because no matter what happens, the child being alive is better than not. However, other parents may view the reduction of pain and suffering as serving the child's best interest. This may mean forgoing experimental therapies that have potential to extend the child's underlying condition, thus extending any pain and suffering associated with this condition. Both of these decisions seem reasonable: in one the parent views the best interest of the child as staying alive as long as possible and the other views the best interest as reducing pain and suffering. While it is rarely a zero-sum game and these decisions are not always in direct opposition to one another, it is possible to envisage a situation in which this were the case.

The second consideration that makes it difficult to apply the best interest standard in end-of-life situations is the fact that parents may not be able to clearly see the best interests of their child due to their own grief.[53] "The primary obligation of a parent is to keep their children healthy, protected and safe" and the end-of-life medical care of a severely ill child threatens all of these obligations. As suggested by Jonathan Santoro and Mariko Bennett, it "may be too optimistic" to

[52] Cornfield and Kahn, "Decisions about Life-Sustaining Measures in Children."
[53] Santoro and Bennett, "Ethics of End of Life Decisions in Pediatrics."

expect parents to focus on the best interests of the child when "confronted with life-altering changes for the child."[54] While parents protective role should be respected, this role "must be balanced and possibly tempered with sound medical practice that weighs quality of life and realistic expectations of outcomes."[55] For this reason, the best interest standard may not be the appropriate guide for decision-making in these circumstances because it does not adequately moderate the duty of the parent.

Constrained Parental Autonomy

Following the initial work by Buchanan and Brock, there has been a robust dialogue surrounding the use of the best interest standard guiding pediatric decision-making. Lainie Friedman Ross critiqued the BIS as ineffective for both a guidance and intervention principle and argues instead for a model of constrained parental autonomy.[56]

> Constrained parental autonomy is a decision-making model that recognizes the wide scope afforded to the authority of the parents, but constrains this autonomy to protect children from parental exploitation, abuse, and neglect, as well as to ensure that parents provide children with the basic interests or needs necessary to create and implement their own life plan.[57]

While parents remain the appropriate decision-maker for their child, their autonomy should be limited by what Ross calls the "modified principle of respect for persons.[58] This model respects the child as they are but also the child they are becoming.[59] This is important because it recognizes that children have both interests that are closely tied to those of their parents as well

[54] Santoro and Bennett.
[55] Santoro and Bennett.
[56] Lainie Friedman Ross, "Better than Best (Interest Standard) in Pediatric Decision Making," *The Journal of Clinical Ethics* 30, no. 3 (2019): 183–95.
[57] Ross.
[58] Ross.
[59] Ross.

as distinct interests that should be considered in medical decision-making.

Constrained parental autonomy is one way to balance and temper the role of parents in end-of-life decision making. While it would be mistaken to claim that a parent's interests are not intimately tied to those of their child, I argue that the interests of the parent should be moderated in end-of-life situations to maximize the well-being of the child. The child's distinct interests should take priority during end-of-life decision making, particularly in the age of medical innovation. These distinct interests include "[helping] them attain the capacity to act autonomously; i.e. to pursue a lifeplan worth living or… to flourish."[60] Due to the significant uncertainty associated with experimental treatments, it is not certain if choosing them would advance these capacities. Decisions that fully competent adults can make for themselves cannot always be ethically made on behalf of their children. This includes "decisions that involve a certain degree of self-sacrifice."[61] Adults can choose to consent to unknown risk for the hope of potential benefit, but we owe it to young pediatric patients to reduce suffering and protect the prospect of a good death. Constrained parental autonomy allows for the potential of oversight in these situations to ensure the interests of the child are being maximized.

The Role of the Physician

Many factors affect a parent's decision whether or not to pursue potentially live sustaining treatment, including "education level, ethnicity, and lack of prior exposure to death of a relative."[62] In addition to the various life experiences that influence parents' decision-making, physicians also shape the end-of-life experience. Although parents are the primary decision

[60] Lainie Friedman Ross, "Moral Grounding for the Participation of Children as Organ Donors," *Journal of Law, Medicine & Ethics* 21, no. 2 (1993): 251–57, https://doi.org/10.1111/j.1748-720X.1993.tb01248.x.
[61] Ross, "Better than Best (Interest Standard) in Pediatric Decision Making."
[62] Santoro and Bennett, "Ethics of End of Life Decisions in Pediatrics."

makers for their children, physicians play an essential role in facilitating end-of-life decision-making and care. To further understand the physician's role, Adrienne Randolph and colleagues conducted a study to investigate how physicians in the pediatric intensive care unit (PICU) went about making decisions relating to pediatric life support. This study included responses from 270 physicians in 29 US PICUs. They found that "respondents considered the probability of ICU survival and the wishes of the parents regarding the aggressiveness of care most important in the decision to limit life-support interventions."[63] This suggests that even though physicians must make medically sound decisions, they "were more likely to choose aggressive care when parents wanted it, even when the long-term prognosis was poor."[64] This indicates that the preferences of parents, and the decisions they make, are highly influential to the course of treatment. Although the Randolph et al. found parental wishes as central to physicians' decision-making process, they also found that variability in how physicians would respond in different scenarios remained. Additionally, the preferences and intensity of care requested by parents are likely affected by how physicians communicate prognosis and treatment options.

If parents make their decisions at least in part due to what is communicated to them by physicians, physicians must consider how they frame various treatment and end-of-life options. Working toward some level of standardization of physician communication would be beneficial as "variability in decision-making may lead to unnecessary suffering, lack of fairness when making decisions about neurologically handicapped individuals, and inappropriate use of scarce resources in futile cases."[65] By ensuring that physicians frame prognosis, treatment, and end-of-

[63] Adrienne G. Randolph et al., "Variability in Physician Opinion on Limiting Pediatric Life Support," *Pediatrics* 103, no. 4 (April 1, 1999): e46–e46, https://doi.org/10.1542/peds.103.4.e46.
[64] Field, Behrman, and Institute of Medicine (U.S.), *When Children Die*.
[65] Randolph et al., "Variability in Physician Opinion on Limiting Pediatric Life Support."

life options consistently, parents are able to make more informed decisions regarding what course of treatment to pursue. So as not to unduly influence a parent's decision, physicians should fully consider their authority in treatment of children with life limiting conditions and the extent to which their communication with parents influences decision-making. It is also essential to remember that this relationship works in both directions: the physician's communication influences the parent's preferences and the parent's preferences in turn have significant influence on the course of treatment the physician ultimately pursues.

The Role of Hope at the End of Life

"One definition of hope is 'a confident yet uncertain expectation of achieving a future good which, to the hoping person, is realistically possible and personally significant."[66] Patients put faith in science and their doctors because it may help them see a future. There exist significant examples of medical advancements bringing hope to patients. For example, when developments in organ transplantation made lung transplants a viable option for patients with cystic fibrosis, what was "previously seen as the end stage of their disease" became "an opportunity to be listed for transplant, thus maintaining hope of survival rather than preparing for death."[67] Now organ transplantation, though still with risks, is part of expected course of treatment for certain conditions. However, at one point, this procedure was the forefront of medical innovation and families were placing hope in a treatment with potentially more risks than benefit. Now a patient can reasonably expect that a lung transplant will be beneficial for them should they make it to the top of the list. Had early patients not participated in trials and

[66] Josephine M. Clayton et al., "Sustaining Hope When Communicating with Terminally Ill Patients and Their Families: A Systematic Review," *Psycho-Oncology* 17, no. 7 (July 2008): 641–59, https://doi.org/10.1002/pon.1288.
[67] Field, Behrman, and Institute of Medicine (U.S.), *When Children Die*.

innovative surgeries, organ transplantation would not be the life-saving procedure it is today.

Considering this example, it is not unreasonable for innovation to provide hope. However, the question remains how this hope should factor into the decision-making process, especially in the case of young pediatric patients who may not benefit from the hope in the same way as adult patients? A review by Josephine Clayton and colleagues found that "patients still expressed a need for hope when they knew and accepted they were in the terminal phase of their illness."[68] This suggests that hope is not always about striving for a cure but maintaining quality of life and positive affect during the dying process. Additionally, hope can be framed by healthcare providers in ways that do not necessitate a cure. Physicians can help foster hope by discussing realistic goals, managing symptoms, and supporting a positive end-of-life experience.[69]

Bryan Sisk and colleagues also studied parental hope by surveying parents and physicians of children with cancer.[70] Their findings supported the concept that hope is a multidimensional experience and hope for a cure was just one aspect that brought hope to parents. Other "child-focused hopes" that contribute to the parent's hopefulness included: "'hope that my child will always feel loved'… 'hope that I will always do everything I can for my child'… and 'hope that my child will have the best quality of life possible.'"[71] Additionally, Sisk and colleagues suggest that "parents view hope as a duty or responsibility of being a 'good parent.'"[72] This implies that if parents' want to fulfill their duty to be a good parent, they ought to have hope for their child.

[68] Clayton et al., "Sustaining Hope When Communicating with Terminally Ill Patients and Their Families."
[69] Clayton et al.
[70] Sisk, Kang, and Mack, "Sources of Parental Hope in Pediatric Oncology."
[71] Sisk, Kang, and Mack.
[72] Sisk, Kang, and Mack.

However, they do not specify what types of hope fulfill these duties of a good parent. From these studies, it is clear that hope can be a fundamental part of the dying process for children and their parents. Physicians and others involved in the end-of-life process of a child should strive to understand what parents are hoping for and support the elements of hope that center the child's interests. "Clinicians should worry less about diminishing hope with honest communication and focus more on supporting the myriad of hopes that contribute to overall hopefulness" and help parents fulfill their obligation of being a good parent. Clinicians and parents must appreciate the different forms of hope while being especially cognizant of the link between hope and experimental therapies, which may disproportionately inflate the hope for a cure.

The Cost-Benefit Analysis of Innovation

Understanding that parental preferences often drive the direction of treatment, parents must ultimately make the cost benefit analysis regarding experimental treatments. Enrolling in an early stage trial, accessing an experimental treatment outside of trials, or undergoing a new surgical approach comes with sacrifice on the part of the patient and their family. The child assumes risk to contribute to the development of scientific knowledge or in the name of hope. Most people agree that the development of new pediatric treatments is beneficial because it is good for children to live longer, healthier lives with improved quality of life. However, to get to the place where these treatments are safe, effective, and accessible on a wider scale, some children will receive the treatment before it is deemed safe and effective. It should be recognized that early phase trials still hold some possibility of benefit to the patient. However, more unknowns about safety and effectiveness exist in these early stage trials than therapies further along in development. Unlike an adult enrolling in a clinical trial or seeking an unapproved treatment, young children do not evaluate the risks and benefits associated with this course of

treatment for themselves. Instead, their parents do so on their behalf. As previously mentioned, the interests of a child are tightly intertwined with those of their parents, and their parents have an interest in their child living as long as possible. While hope is an important benefit of experimental treatments, it mostly serves to improve the emotional wellbeing of the parents since infants and toddlers cannot yet internalize this hope themselves. Experimental therapies can create the hope for a cure as well as the hope that parents are doing everything they can for their child. This can fulfill the parents desire and obligation to be a good parent.[73] As such, we must be cautious that hope does not unduly tip the scales away from the child's interests. Thomas Felborg, the father of a daughter living with a rare, fatal genetic disorder summed up this tension, saying "There's a fine line between bravery and stupidity. Are we so stupid in our hope? Is it a fool's mission we're on?"[74] Parents like Thomas are faced with these questions every day and how they respond has significant consequences for the well-being of their child.

How Should We Move Forward?

The future of medicine depends upon fostering the development of new, effective therapies. Without innovation, children will continue to die from serious conditions early in life. While impressive progress has been made, as exhibited by a 15% decrease in infant mortality from 2005 to 2014, there is still much work to be done.[75] However, the parents and physicians involved in a child's end-of-life care must be careful that hope and medical advancement does not outweigh the prospect of a good death, especially when children cannot advocate for themselves. Despite the positive effects of hope, parents and healthcare professionals must

[73] Sisk, Kang, and Mack.
[74] Karen Weintraub, "An Experimental Gene Therapy Was Little Alissa's Only Hope. Now, Instead of Certain Death, She Faces an Uncertain Future."
[75] T.J. Matthews and Anne K. Driscoll, "Trends in Infant Mortality in the United States, 2005–2014," NCHS Data Brief (National Center for Health Statistics, March 2017).

ensure that hope is effectively balanced with the reduction of harm. This can include prioritizing palliative care, even when choosing to pursue experimental treatments. Palliative care is often misconstrued as synonymous with end-of-life care, but this is not the case. Palliative care is often provided in addition to "disease-directed, cure-seeking, or life-prolonging care" and aims to "palliate symptoms, enhance comfort, and improve quality of life" for the patient.[76] Minimizing harm, and by extension suffering, must be heavily weighted in end-of-life situations where the child lacks the ability to appreciate and communicate their preferences. While it may be reasonable for parents to choose experimental treatments for themselves with the hope of obtaining benefit despite the risk of suffering, they should not assume their child would want the same thing. Parents must achieve the delicate balance between their own desires and minimizing potential harms to their child. Recognizing that there are some interests of children that are distinct from their parents helps keep them at the forefront of the decision-making process. While it may be in the parent's best interest to have their child with them for as long as possible, experimental treatments are not always the best way to respect the interests of the child. Decision-making guided by constrained parental autonomy and a multidimensional understanding of hope protects the interests of the child and provides a safeguard from hope for a cure placing undue influence on the decisions made by parents and the healthcare team.

Conclusion

While experimental treatments and medical innovation can be compatible with a pediatric good death, it is also possible that the hope derived from these treatments can result in added harm to the child if too much weight is given to the hope for a cure. It is critical that the interests and well-being of children with life-limiting and life-threatening diseases are prioritized as we

[76] *Dying in America*.

continue to innovate and make scientific advancements. The question of how the child's interests are balanced with parental interests and scientific advancement should be at the forefront of all medical decision-making.

One way to focus on the child's distinct interests is by prioritizing palliative care. While the child may not have yet developed their own preferences, as a matter of existing there is a natural desire for a life free from suffering. It is clear that a good death involves as little physical and emotional suffering as possible while aligning with the patient's preferences. Since the preferences of very young children remain unknown, those involved in the end-of-life care of these children should focus on ensuring a pediatric good death should by reducing suffering. While every loss of a child is heartbreaking, each end-of-life journey is unique. Experimental medicine has the potential for tremendous curative or life-extending benefits, but all parties involved in the end-of-life care of a child ought to be mindful of the way these potential benefits play into the decision-making process.

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Biographical Statement

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Caroline has spent the past several years working at the National Organization for Rare Disorders, a patient advocacy non-profit organization committed to improving the lives of those living with rare diseases. In her work, she helps develop educational programs and resources to support rare disease patients, caregivers, and medical professionals.